FILE 'BIOSIS' ENTERED [redacted]17:16:30 ON 13 JUN 2000
COPYRIGHT (C) 2000 BIO[redacted](R)

=> s leptin

L1 6146 LEPTIN

=> s l1 and py<1999

L2 3706 L1 AND PY<1999

=> s l2 and (inhibit?)/ti

L3 106 L2 AND (INHIBIT?)/TI

=> s l3 and tumor

L4 11 L3 AND TUMOR

=> dup rem l4

PROCESSING COMPLETED FOR L4
L5 8 DUP REM L4 (3 DUPLICATES REMOVED)

=> d ibib abs tot

L5 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:199888 BIOSIS
DOCUMENT NUMBER: PREV199800199888
TITLE: **Inhibition** of cholecystokinin (CCK)-stimulated amylase release by **leptin** in rat pancreatic **tumor** cells.
AUTHOR(S): Harris, D. M. (1); Flannigan, K. I. (1); Go, V. L. W. (1); Wu, S. V.
CORPORATE SOURCE: (1) Cent. Hum. Nutr., UCLA Sch. Med., Los Angeles, CA 90095
USA
SOURCE: FASEB Journal, (**March 17, 1998**) Vol. 12, No. 4, pp. A260.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology
. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:533595 BIOSIS
DOCUMENT NUMBER: PREV199800533595
TITLE: **Inhibition** of OB gene expression and **leptin** production by chronic TNFalpha treatment of 3T3-F442A adipocytes.
AUTHOR(S): Tadayyon, M.; Haynes, A. C.; Holder, J. C.; Arch, J. R. S.
CORPORATE SOURCE: Dep. Vasc. Biol., Smithkline Beecham Pharm., Harlow UK
SOURCE: International Journal of Obesity, (**Aug., 1998**) Vol. 22, No. SUPPL. 3, pp. S32.
Meeting Info.: Eighth International Congress on Obesity Paris, France August 29-September 3, 1998 International Association for the Study of Obesity
. ISSN: 0307-0565.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 3 OF 8 MEDLINE [redacted] DUPLICATE 1
ACCESSION NUMBER: 19[redacted]183393 MEDLINE
DOCUMENT NUMBER: 98183393
TITLE: Autocrine **inhibition** of **leptin** production by **tumor** necrosis factor-alpha (TNF-alpha) through TNF-alpha type-I receptor in vitro.
AUTHOR: Yamaguchi M; Murakami T; Tomimatsu T; Nishio Y; Mitsuda N; Kanzaki T; Kurachi H; Shima K; Aono T; Murata Y
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Osaka University Medical School, Suita, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1998 Mar 6)** 244 (1) 30-4.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199806
AB The aim of this study was to find factors which regulate m-**leptin** secretion during pregnancy. Mouse parametrial adipocytes from day 13 of pregnancy were cultured with or without mouse placental lactogen (mPL)-I, mPL-II, or mouse **tumor** necrosis factor-alpha (mTNF-alpha) and mouse-**leptin** (m-**leptin**) concentration in the medium was assessed by RIA. Up to four days of mPL-I or mPL-II treatment did not affect m-**leptin** secretion. However, mTNF-alpha, which is produced by adipocytes, significantly inhibited m-**leptin** secretion in a dose- and time-dependent manner. Antibody to mTNF-alpha completely blocked the inhibitory effect of mTNF-alpha on m-**leptin** secretion. mTNF-alpha significantly inhibited the expression of m-**leptin** messenger RNA. Agonistic polyclonal antibody directed against the mTNF-type-I receptor (mTNF-RI) significantly inhibited m-**leptin** secretion, but the anti-mTNF-RII antibody did not change m-**leptin** secretion. Moreover, human TNF-alpha (h-TNF-alpha) also inhibited human-**leptin** (h-**leptin**) secretion by cultured human adipocytes collected from the subcutaneous fat of pregnant women. These results suggest that TNF-alpha, which is secreted by adipocytes, inhibits m-**leptin** secretion through mTNF-RI and suggest the presence of an autocrine or paracrine regulation of **leptin** secretion in human and mouse adipose tissue in vivo.

L5 ANSWER 4 OF 8 MEDLINE
ACCESSION NUMBER: 1998049615 MEDLINE
DOCUMENT NUMBER: 98049615
TITLE: Specific **inhibition** of Stat3 signal transduction by PIAS3.
AUTHOR: Chung C D; Liao J; Liu B; Rao X; Jay P; Berta P; Shuai K
CORPORATE SOURCE: Department of Biological Chemistry, University of California, Los Angeles, CA 90095, USA.
CONTRACT NUMBER: T32CA09056 (NCI)
AI39612 (NIAID)
SOURCE: SCIENCE, **(1997 Dec 5)** 278 (5344) 1803-5.
Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-H58757
ENTRY MONTH: 199802
ENTRY WEEK: 19980204
AB The signal transducer and activator of transcription-3 (Stat3) protein is activated by the interleukin 6 (IL-6) family of cytokines, epidermal growth factor, and **leptin**. A protein named PIAS3 (protein inhibitor of activated STAT) that binds to Stat3 was isolated and characterized. The association of PIAS3 with Stat3 in vivo was only observed in cells stimulated with ligands that cause the activation of

Stat3. PIAS3 blocked the DNA-binding activity of Stat3 and inhibited Stat3-mediated gene activation. Although Stat1 is also phosphorylated in response to IL-6, PIAS3 did not interact with Stat1 or affect its DNA-binding or transcriptional activity. The results indicate that PIAS3 is a specific inhibitor of Stat3.

L5 ANSWER 5 OF 8 MEDLINE
ACCESSION NUMBER: 1998057854 MEDLINE
DOCUMENT NUMBER: 98057854
TITLE: **Leptin**: a potent **inhibitor** of insulin secretion.
AUTHOR: Fehmann H C; Peiser C; Bode H P; Stamm M; Staats P; Hedetoft C; Lang R E; Goke B
CORPORATE SOURCE: Department of Medicine, Philipps-University of Marburg, Germany.
SOURCE: PEPTIDES, **(1997)** 18 (8) 1267-73.
Journal code: PA7. ISSN: 0196-9781.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
AB The hormone **leptin** is expressed and secreted by the adipose tissue and impacts on the central nervous system. **Leptin** is involved in the regulation of energy balance, satiety, and body composition. The lack of active **leptin** results in obesity, high food intake, hyperglycemia, and hyperinsulinemia. We present data supporting effects of **leptin** on the endocrine pancreas. We found the **leptin** receptor to be expressed in insulin- and glucagon-secretin cells derived from mouse, hamster, and rat pancreas. In the isolated perfused rat pancreas **leptin** is a potent inhibitor of basal and glucose-induced insulin secretion, especially during the first phase of the insulin response. At isolated mouse islets and insulin-secreting INS-1 cells **leptin** reduced promptly and persistently the intracellular Ca2+ levels. Cytoplasmic Ca2+ oscillation amplitude was decreased and the oscillation frequency increased. These findings suggest functional active receptors for **leptin** on insulin-secreting B-cells. Therefore, **leptin** is a metabolic hormone and not only a signal to the brain indicating filled fat stores. Our data suggest that **leptin** is also a signal back to the endocrine pancreas that no more insulin is required to replenish fat stores. Thus, an "adipo-insular axis" operating with two arms exists: insulin and glucagon are signals to the adipocyte. This releases **leptin**, which could be the mediator of the respective feedback to the pancreas. A defective **leptin** suppression of insulin secretion could contribute to hyperinsulinemia and disturbances of glucose metabolism.

L5 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:69560 BIOSIS
DOCUMENT NUMBER: PREV199800069560
TITLE: **Leptin inhibits** growth-factor-induced cell proliferation.
AUTHOR(S): Rubinstein, M.; Barkan, D.; Cohen, B.; Novick, D.
CORPORATE SOURCE: Weizmann Inst. Science, Rehovot 76100 Israel
SOURCE: Cytokine, (**Nov.**, **1997**) Vol. 9, No. 11, pp. 953.
Meeting Info.: Fifth Annual Conference of the International Cytokine Society Lake Tahoe, Nevada, USA November 9-13, 1997 International Cytokine Society
. ISSN: 1043-4666.
DOCUMENT TYPE: Conference
LANGUAGE: English

L5 ANSWER 7 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97278979 MEDLINE
DOCUMENT NUMBER: 97278979
TITLE: Production of plasminogen activator **inhibitor** 1 by human adipose tissue: possible link between visceral fat accumulation and vascular disease.
AUTHOR: Alessi M C; Peiretti F; Morange P; Henry M; Nalbone G; Juhan-Vague I
CORPORATE SOURCE: CJF, Institut National de la Sante et de la Recherche Medicale (INSERM), Laboratoire d'Hematologie, Marseille, France.
SOURCE: DIABETES, **(1997 May)** 46 (5) 860-7.
Journal code: E8X. ISSN: 0012-1797.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199707
ENTRY WEEK: 19970705
AB Plasminogen activator inhibitor type 1 (PAI-1) contributes to the pathogenesis of atherothrombosis. Its plasma level is strongly correlated with parameters that define the insulin resistance syndrome, in particular with BMI and visceral accumulation of body fat, suggesting that PAI-1 may be an adipose tissue-derived circulating peptide. The present study was designed to investigate PAI-1 expression by human adipose tissue and its different cellular fractions. Special interest has been paid to the amount of PAI-1 antigen produced by omental versus subcutaneous fat. PAI-1 protein detected by immunolocalization was present at the stromal and adipocyte levels. PAI-1 mRNA was detected in stromal vascular cells freshly isolated and under culture conditions. It was also detected in whole adipose tissue and adipocyte fraction under culture conditions. The mRNA signal from the adipocyte fraction was detected as early as 2 h of incubation. The increase in PAI-1 mRNA was followed by an increase in PAI-1 antigen in the conditioned medium that was suppressed by treatment with cycloheximide. Transforming growth factor-beta1 significantly increased PAI-1 antigen production by the adipocyte fraction, whereas **tumor** necrosis factor-alpha did not have any effect. Interestingly, after 5 h of incubation, omental tissue explants produced significantly more PAI-1 antigen than did subcutaneous tissue from the same individual, whereas similar production of **leptin** by the two territories was observed. These results strongly suggest that human adipose tissue, in particular visceral tissue, can be an important contributor to the elevated plasma PAI-1 levels observed in central obesity.

L5 ANSWER 8 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998049840 MEDLINE
DOCUMENT NUMBER: 98049840
TITLE: Transforming growth factor-beta enhances and pro-inflammatory cytokines **inhibit** ob gene expression in 3T3-L1 adipocytes.
AUTHOR: Granowitz E V
CORPORATE SOURCE: Department of Medicine, Baystate Medical Center, Springfield, Massachusetts, USA.. granowitz@bmcsouth.bhs.org
CONTRACT NUMBER: AI-01288 (NIAID)
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1997 Nov 17)** 240 (2) 382-5.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 1[redacted]02

AB **Leptin** is a protein which is encoded by the obese (ob) gene. It is synthesized by adipocytes and binds to receptors in the hypothalamus, thereby suppressing appetite and increasing the metabolic rate. When mouse 3T3-L1 cells are induced to differentiate into adipocytes, they begin to constitutively express low levels of ob mRNA. Using reverse transcription and a semi-quantitative polymerase chain reaction, the experiments described herein demonstrate that the anti-inflammatory cytokine transforming growth factor-beta increases steady state ob mRNA. Conversely, treatment of 3T3-L1 adipocytes with the pro-inflammatory cytokines interleukin-1 beta, interleukin-6, interleukin-11, and **tumor** necrosis factor-alpha results in a decrease in ob transcripts. When considered in the context of animal studies showing that interleukin-1 and **tumor** necrosis factor-alpha induce **leptin** and ob mRNA, these results suggest that pro-inflammatory cytokines induce ob gene transcription in vivo via secondary mediators such as transforming growth factor-beta.

=> display history l1-l5

ENTER (BRIEF) OR FULL:brief

(FILE 'MEDLINE, BIOSIS' ENTERED AT 17:16:30 ON 13 JUN 2000)

L1 6146 S LEPTIN
L2 3706 S L1 AND PY<1999
L3 106 S L2 AND (INHIBIT?)/TI
L4 11 S L3 AND TUMOR
L5 8 DUP REM L4 (3 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.00	9.15